SUPPLEMENT ARTICLE

Perspectives on Introduction and Implementation of New Point-of-Care Diagnostic Tests

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In recent years, there has been significant investment from both the private and public sectors in the development of diagnostic technologies to meet the need for human immunodeficiency virus (HIV) and tuberculosis testing in low-resource settings. Future investments should ensure that the most appropriate technologies are adopted in settings where they will have a sustainable impact. Achieving these aims requires the involvement of many stakeholders, as their needs, operational constraints, and priorities are often distinct. Here, we discuss these considerations from different perspectives representing those of various stakeholders involved in the development, introduction, and implementation of diagnostic tests. We also discuss some opportunities to address these considerations.

Both human immunodeficiency virus (HIV) and tuberculosis disease programs have been innovative in developing systems for taking complex treatment algorithms closer to patients, even to those in remote areas where healthcare access is limited. HIV programs have been remarkably successful in providing access to treatment. However, early case detection remains a bottleneck in HIV and tuberculosis control [1–3], even with the availability of extremely good and inexpensive point-of-care (POC) tests for HIV diagnosis [4].

Beyond case detection, HIV and tuberculosis have multiple and challenging requirements for diagnostic testing, which are further complicated by the high levels of drug resistance already present and emerging for both diseases. Additionally, the high rates of HIV and tuberculous mycobacteria coinfection in many countries complicate diagnosis and management. For multiple reasons, including a potentially high-value market in the developed world, the diagnostics community has responded by developing tests to meet the needs of HIV programs, albeit in platforms not always appropriate for low-resource settings. For tuberculosis, a much more donor-driven effort has been required to advance the development of needed diagnostic tests [5, 6]. A historical perspective of diagnostics development for HIV, tuberculosis, and malaria is strongly suggestive of different parameters, including market forces, driving the development of in vitro diagnostic laboratory tests and POC rapid tests for these 3 diseases. Only 2 malaria tests have been approved by the US Food and Drug Administration (FDA), in contrast to approximately 20 tests for tuberculosis and >30 tests for HIV (Figure 1). Notably, the first rapid test for malaria was approved approximately 15 years after the first in vitro diagnostic product of its class hit the market. Several factors may contribute to the differences highlighted in Figure 1, including the absence of

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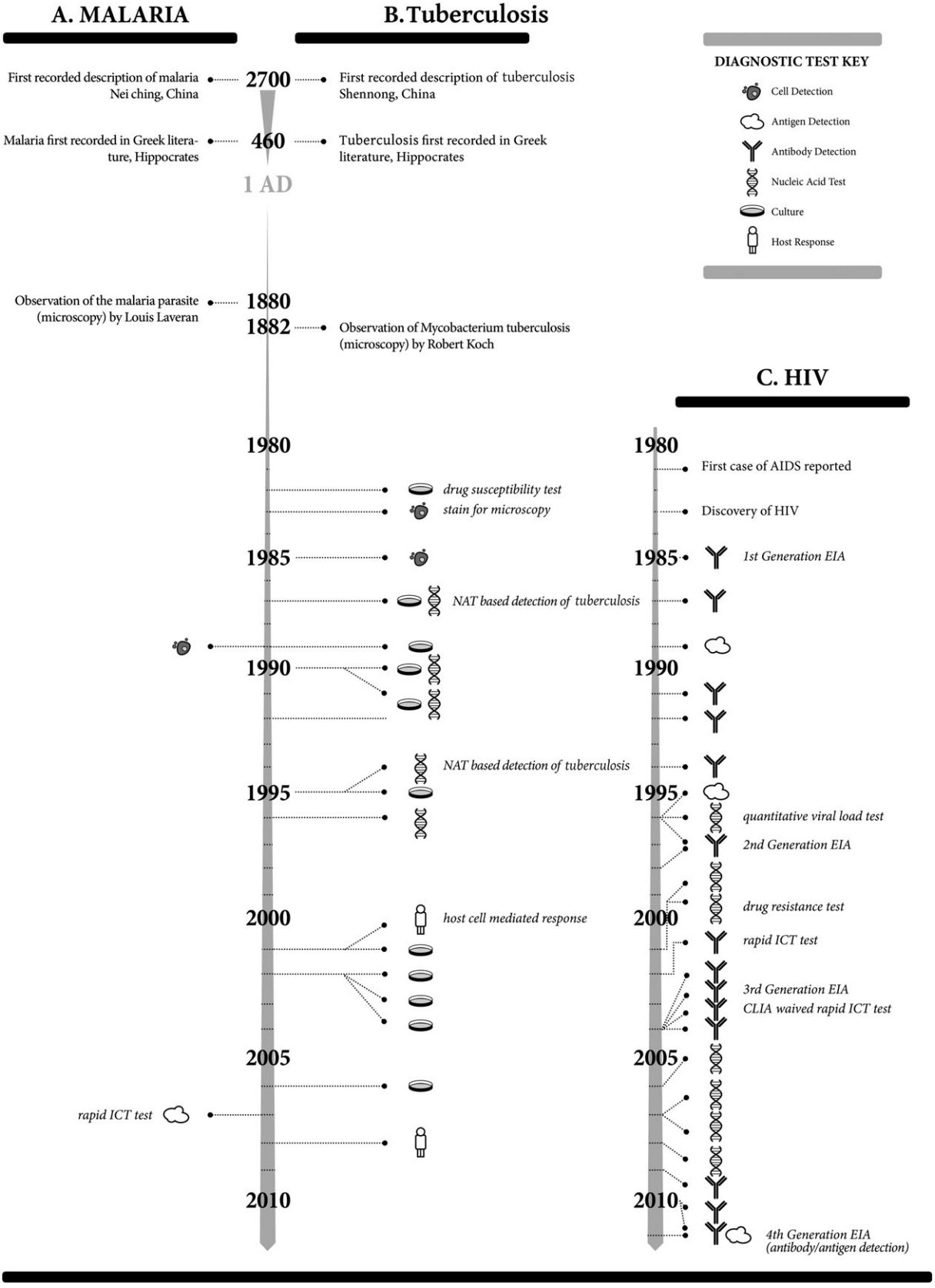

Figure 1. Historical perspective on diagnostic tests for malaria (*A*), tuberculosis (*B*) and human immunodeficiency virus (HIV; *C*) in the context of first recorded observations of disease, identification of pathogen, and approval from the US Food and Drug Administration. Abbreviations: EIA, enzyme immunoassay; ICT, immunochromatography test; NAT, nucleic acid-based test.

a local market (in the case of malaria); historically less cohesive policy, regulatory, and funding strategies (in the case of tuberculosis); a broader socioeconomic target market (in the case of HIV); and inherent technical challenges for developing appropriate diagnostic tests (more so for tuberculosis than for HIV).

Implementation of these products in low-resource settings is a major challenge, particularly for the goals of using the tests to enhance clinical decision making and of improving access to the tests by people who need it. Most notably, the cost of POC diagnostic testing is chronically underestimated when the additional costs of implementation, staffing, training, and maintenance are excluded from "cost per test" calculations [7]. Despite this, both for HIV and tuberculosis, complex and costly diagnostics are being implemented in settings where even microscopy-based diagnosis is considered a technical and financial challenge. Perhaps the strongest example of this is CD4 cell count testing by flow cytometry, which has evolved in a space of approximately 30 years from a central laboratory research tool to a platform for decentralized facilities, including district hospitals in remote settings, with the volume of tests performed significantly driving the cost of the tests down [8]. Both private-sector initiatives and donor-driven initiatives, such as the CD4 Initiative [9], have spurred innovation in CD4 cell count testing to specifically address the needs in low-resource settings [10]. Despite the evidence of failed attempts to decentralize CD4 cell count testing, in the form of unused instruments in primary and secondary hospitals, CD4 cell count testing platforms are significantly more available at lower-tier laboratories than platforms for determining viral load, such as nucleic acid–based testing (NAT) platforms [11]. Innovative POC platforms are taking CD4 cell count testing to settings unattainable by centralized testing systems [12–14]. In the tuberculosis community, a NAT-based platform is being introduced into lower-tier laboratories at an unprecedented rate [15–17].

In contrast to the rapid tests for HIV and malaria, one significant implementation barrier for current POC CD4 cell–based and NAT-based tuberculosis and HIV tests is the requirement of instrumentation for these platforms. The transport, calibration, and maintenance of instrumentation poses additional barriers to implementation of these tests in remote settings, but the tests also provide opportunities for improving care, such as digital information recording and transmission.

A major issue for program implementers is the sustainability of POC testing programs. The appropriate solutions must address many of the processes involved in implementing and performing diagnostic testing, including an appropriate match of the tests to POC health systems and laboratory systems, the skill sets of the local workforce, and the operation of the tests themselves. Here we discuss different barriers to the introduction of appropriate POC diagnostic technologies, presented from the perspectives of different stakeholders, and we review opportunities to address these barriers.

BARRIERS TO INTRODUCTION OF NEW TECHNOLOGIES

There are many barriers to overcome in order to transition a product from development to introduction and implementation. From the perspective of the supplier (the product developer and marketer), most of these barriers arise from uncertainty around the information required to demonstrate the value of the test for those who might demand it (test purchasers, end users, and patients). From the demand perspective, perhaps the greatest barrier is the availability of resources required to support (1) the evaluation of new technologies for performance in clinical and POC settings; (2) the evaluation of operational viability, including costing and modeling; and (3) the adjustments to health and laboratory systems necessary to ensure effective adoption and implementation of the tests. In Table 1, we summarize some of the barriers to introduction of new POC diagnostic tests; barriers to implementation have been summarized by Schito et al elsewhere in this supplement of *The Journal of Infectious Diseases* [7].

It is critical to address these barriers, as they represent a disincentive to the supply side to develop innovative technologies that challenge the status quo and meet current and emerging unmet needs. From the demand side, the barriers represent a disincentive to absorb new but potentially more cost-effective solutions. Barriers to the adoption of new technologies can be analyzed from the perspective of the various stakeholders by organizing them into components of a framework for product introduction and implementation.

Policy

In the past, on recognition of the urgent need to provide antiretroviral treatment (ART) to individuals with advanced disease, the World Health Organization (WHO) produced guidelines that recommended presumptive therapy, in which clinical criteria were used to determine the time of ART initiation and to monitor patients during therapy in settings where immunologic and virologic testing was not available [18]. Increasing evidence points to the importance of initiating treatment *before* the development of clinical disease, in both adults and children. A number of cohort studies and randomized clinical trials have shown that early initiation of ART for HIV infection decreases mortality, morbidity, and the incidence of tuberculosis [19–25]. In keeping with this evidence, WHO recommendations have evolved, and although the guidelines still offer the option of initiating treatment on the basis of clinical criteria, the emphasis has shifted toward increased use of CD4 cell count testing, to determine treatment eligibility, and increase use of viral load testing, to evaluate treatment failure. There is recognition of the importance of diagnostic testing for HIV management and of the need to strengthen laboratory systems, as expressed in the Maputo Declaration [26, 27]. Clearer policy guidelines would

Table 1. Barriers and Opportunities to Introduction of Point-of-Care (POC) Diagnostic Tests to Low Resource Settings (LRSs)

Barriers	Impact on Supply	Impact on Demand	Opportunities
Ambiguous policy on use of diagnostics for clinical management	Undefined market opportunities and uncertainty in demand projections	The value proposition for adoption of a diagnostic test is undermined	Clearer policy guidelines with respect to diagnostic testing need to be established
Fragmented, unclear, and complex regulatory and registration processes at both international and national levels	Difficulty in mapping the most effective route to product registration when targeting to multicountry markets	In absence of clear international regulatory standards, procurers default to inappropriate regulatory standards	Where possible, regional regulatory and registration processes could be harmonized
Inconsistency between policy recommendations and regulatory standards	Leads to ambiguous product specifications and can lead to overdesigned, costly products	Leads to ambiguous criteria by which to evaluate technologies	Regulatory standards need to be harmonized with policy guidelines and publicized
Absence of robust and standard indicators/metrics to assess the impact of POC diagnostics tests beyond analytical performance	Challenge to demonstrate the value proposition for a POC product	No way of assessing the benefits of a new POC test when matched against central laboratory test	Investment is needed in fundamental operational research and modeling; local operational research capacity needs to be built
Inconsistency in purchasing practices from the donor community and national program	Leads to ambiguity in target price points and product specification trade-off decisions	Disenfranchises the end user (national laboratory systems) and patient as key stakeholders in defining product attributes and adoption decisions	Standards for assessment of impact and appropriateness of new POC technologies need to be developed and disseminated to key stakeholders
Poor definition of market opportunities	Challenging to define appropriate product profiles and specifications; disincentive to develop products specifically for LRS	A weak product pipeline, and products in the pipeline are often not appropriate for the end user; decision making for adoption of new technologies is poorly informed	Rigorous market intelligence needs to be collected and appropriately disseminated to key stakeholders
Undeveloped market environment	High uncertainty in timelines for product introduction and scale-up		

greatly assist the supply side in defining needs and opportunities, target markets, and target product profiles—not just in terms of defining where tests are required but also in clarifying the performance characteristics of tests in specific settings. Conversely, from the demand perspective, better-defined global standards would also help to strengthen local regulatory priorities for evaluation and implementation of new diagnostics.

HIV load testing for patients receiving ART is a useful case in point. There is increasing evidence for the usefulness of viral load in assessing response to and changes in therapy [19, 22, 28]. At present, recommendations on the use of viral load for patient monitoring are "conditional"; in other words, they are not necessary for implementation in all settings. Stronger policy recommendations would reduce the market uncertainty and incentivize companies to develop products for use in this area. Additionally, in the absence of clearly defined clinically relevant performance criteria for resource-limited settings, stakeholders may default to FDA regulatory standards, which call for viral load assays to be quantitative and highly sensitive with a very low limit of detection. While the performance of a test should not be compromised the standards by which it is evaluated should reflect the clinical need in the target settings.

Regulatory Requirements

The regulatory requirements for introduction of diagnostic tests into multiple countries remain a major challenge. Suppliers must accommodate multiple regulatory standards and processes (or, in some countries, the absence of regulatory processes altogether) and/or default to regulatory processes that may be insufficient or inappropriate for specific settings. The ambiguity in regulatory approval leads to uncertainty on both the supply and demand sides, results in redundancy in regulatory approval processes, and may result in a disincentive to develop appropriate technologies.

In the absence of WHO prequalification and/or a national regulatory process, one option is to require regulatory approval from the country of origin or via an external stringent regulatory authority. However, it is important to understand the context of that regulatory approval. In the case of a test approved by the FDA, for example, there is assurance of the quality of the test and a well-controlled manufacturing process. However, the clinical performance (ie, sensitivity and specificity) is based on data from studies conducted primarily (and often exclusively) within US populations and settings. When the test is used in non-US populations, sensitivity and specificity may differ substantially, depending on the heterogeneity of the analyte (eg, HIV type 1 subtypes) and population/environmental differences, respectively [29–32]. Therefore, adopting an approach that relies on prior FDA approval, for example, will necessarily require additional field trials to demonstrate test performance in other settings. Such a requirement may present an insurmountable resource hurdle, effectively discouraging companies from targeting the international global health market.

Developing regional regulatory processes may be a useful solution, following the European model [33], but this approach requires consensus from a broad set of stakeholders, with accompanying challenges. The WHO Prequalification of Diagnostics Programme [34] is also an attractive proposition for providing assurance about a product's high quality, if there are adequate resources available for the program to develop the agility and responsiveness to evaluate technologies as they emerge, in a timely manner.

One approach that has seen some success is the coordination of test development. For example, through coordinated efforts led by the Stop TB Partnership, the Foundation for Innovative New Diagnostics, and the WHO, excellent guidelines for the use of tuberculosis diagnostics, including emerging diagnostics, have been developed [1, 35]. This, in turn, has resulted in the rapid endorsement of new technologies by the WHO, thus facilitating the introduction of these tests [1, 35, 36].

There is a need for development of transparent, sustainable, and efficient regulatory processes that assess product quality and implementation and ensure controlled, high-quality manufacturing process. With a better-defined market opportunity and regulatory process, there would be greater incentive for suppliers to sustain appropriate supply chains. A single solution is unlikely to emerge given the geopolitical diversity in global markets and the impact of infectious agent diversity on test performance.

Operations Research

Operations research is an interdisciplinary science that focuses on measuring the net effect of technology in the field—in this case, HIV and tuberculosis POC testing technologies by health systems. There is evidence suggesting that new POC HIV and tuberculosis tests provide a variety of operational benefits over existing, central laboratory–based testing, including increasing the number of individuals who actually receive their test results [37–40]. These operational benefits, however, may not be prioritized by local or regional regulatory authorities when deciding to approve and adopt a new test. Rather, the regulatory approval process for many countries begins and ends with a technical evaluation process developed for existing laboratory tests long before POC tests existed. For these technical evaluations, the sensitivity and specificity of a new test are compared with those of the laboratory reference standard. If the new test does not meet or exceed this standard, then often it is not approved or even considered by the regulatory authority.

As the number of new POC tests increases, regulatory authorities should consider supplementing traditional technical evaluations with an operational component. A POC technology may not be as sensitive or specific as the approved reference standard, but it may net important public health benefits through the ability to test in settings where standard laboratory testing is unattainable. An operational evaluation would help quantify this net benefit. For example, a hypothetical new POC

test for diagnosing HIV infection in infants with >90% sensitivity and >90% specificity "could transform current treatment standards by identifying more infants in need of care, thereby allowing providers to expand beyond treating only the most severely ill and paving the way for earlier treatment" [41]. This hypothetical test for early infant diagnosis (EID) of HIV infection, however, would not meet the WHO 2010 Recommendations on the Diagnosis of HIV Infection in Infants, which recommend a POC EID test with a "sensitivity of at least 95% and ideally greater than 98% and specificity of 98% or more under quality-assured, standardized, and validated laboratory conditions" [42]. A local regulatory authority would not approve the new POC EID test because it would fail the technical requirements, despite the obvious benefits that any POC EID test would bring, such as same-day results, reduced loss to follow-up among patients, and evidence-based treatment strategies. In fact, the addition of an operational component may prove the new POC EID test to be *more* effective than the existing reference standard if it enables more HIV-positive infants to receive a diagnosis and initiate proper treatment sooner.

If a device is deemed acceptable by both a technical and operational evaluation, a decision maker is then tasked to determine how and where to place the device within a health systems network. Given that POC devices cannot be placed in all facilities because of budget constraints, they often coexist with standard laboratory-based testing in part of the network, at least in the initial stages of implementation. In such situations, it is important to understand how deployment of a new POC device would change the diagnostic delays within the broader network—particularly if it helps alleviate a throughput bottleneck of a centralized testing facility—and thereby change access to and effectiveness of therapy. The combined technical and operational evaluations would require a multidisciplinary team, which can be challenging and expensive to assemble. As POC technologies become more widely available, however, investments in operations research become increasingly important. Unfortunately, very few countries can afford to commit resources to this type of research. However, strengthening the in-country or regional capacity to perform this evaluation would empower the purchase decision-making process and proactively influence the product profiles to meet country needs.

Procurement

Robust procurement systems are key to effective implementation of new technologies, especially when components of the technologies, such as the reagents and quality control panels, have limited shelf lives and frequently require cold-chain support. Weak procurement systems place a burden on both the supply side and the demand side constituents. While procurement systems should be strengthened, technology developers targeting these settings need to adhere to product specifications that reflect these constraints.

Trained staff and appropriate information systems are essential to procurement systems because they enable accurate forecasting and rational and timely purchasing. In the absence of these, programs have a tendency to perform bulk purchases, often at irregular intervals. This places a burden on the supply side, which must dedicate its manufacturing capacity to meet these large one-time purchases. On the demand side, forecasting miscalculations lead to gross inefficiencies that can result in an oversupply of expired reagents or "stock-outs" when supplies cannot be replaced in a timely manner. Timely and distributed procurement strategies allow manufacturers to plan for provision of supplies with longer time-to-expiration periods, through distribution channels that are more cost-efficient (eg, sea vs air).

Strengthening of procurement systems is critical for long-term implementation of high-value diagnostic tests. Unlike the centralized procurement process for therapeutics, in many countries the procurement of diagnostics is decentralized and specific to the hospital or clinic where it will be used. A case has been made for an approach to centralizing diagnostic test purchasing via a set of standard procurement requirements [11]. Greater levels of centralization (or at least coordination) enable bulk purchase negotiations, a benefit to the demand side [43]. It is important for such mechanisms to include a process for adoption of new technologies and to safeguard against the potential for a supplier monopoly.

Distribution

Procurement and distribution systems are interdependent and must be equally effective to ensure availability of diagnostic tests to the end users. Product characteristics such as the shelf life of reagents and control panels can withstand weaknesses in either of these systems but only to a limited extent. While procurement contracts may be able to induce commitment from the supplier, there must also be effective in-country distribution systems. There are multiple potential bottlenecks in the implementation of effective distribution systems and subsystems involved, including a lack of human resources, weak information management systems to track inventory, overburdened healthcare facilities, and slow administrative processes for requisitions of laboratory tests. Addressing these shortcomings will be critical with the introduction of high-value products such as the current CD4 cell count, viral load, and molecular diagnostic tests for tuberculosis case detection, given the resulting added cost of weak distribution chains on the impact of these tests.

Service, Maintenance, and Repair

Under ideal circumstances in high-resource settings, maintenance and repair services for instrumentation are not insignificant expenses because they are typically implemented as an additional service contract between suppliers and end users. Implementation of service in resource-limited settings presents a logistical challenge beyond the additional cost. New instrumentation and

technology for remote connectivity may address some of the POC challenges through linkage to laboratory-information systems. However, the need for maintenance and repair presents a major barrier to implementation in remote areas where these tests are most needed.

For successful implementation, additional support must be considered for (1) the high cost for service contracts (and any additional costs for repair) to remote regions and (2) the skill set required for routine service. Transparency of these costs and negotiated pricing will go a long way toward addressing this aspect [1, 44]. Another aspect is the cost to the supply side to implement a functioning maintenance and repair system. A service agreement is meaningless if the service is not accessible. For companies with multiple instruments targeting the same market or with common platforms for multiple applications, providing service may be a sustainable proposition. While the new POC systems are designed to require less service and support, new maintenance and service models need to be considered.

In addition to onsite service calls, an effective means of providing laboratory instruments support is to implement a ''warm line,'' wherein the company calls each laboratory on a monthly basis. By using this approach, the company can determine whether the person who was trained to run the system is still employed, whether the laboratory has the consumables required to run the test, and/or whether the instrument itself is operational or broken.

Training and Sustaining Proficiency of Staff

The need for training in performing a diagnostic test, both in terms of initial training and ongoing proficiency training and evaluation, is a chronically underestimated component of the implementation of POC diagnostic tests [45–49]. A test that is easy to use and allows less skilled workers to perform it is systematically misunderstood as obviating the need for training and continuous monitoring of user capacity. One result is that even the simplest POC tests are performed incorrectly and misinterpreted, resulting in low operational test performance. In fact, the training requirements are often greater and need to include aspects such as good laboratory practice, quality control, safety, and instrument maintenance. Another area that requires simplification and training is the clinical algorithm and an understanding of the rationale for the test and interpretation of the results.

POC tests often fail at the interface of laboratory and health systems. Even in a single country, laboratory technicians may perform certain tests in some contexts, while healthcare workers perform the same tests in other contexts. This brings challenges to assigning ownership of user training and monitoring of user proficiency. Again, innovative training models are required that ensure the proficiency of users in already overburdened healthcare systems with limited resources. As instrumentation becomes more widely accepted as part of the decentralized laboratory system, is there an opportunity to develop new and sustainable training tools?

Quality Assurance and Quality Control

A critical component of ensuring that a diagnostic test will have a beneficial impact is quality assurance. Historically, for low-cost diagnostic tests such as microscopy and rapid tests for malaria diagnosis, quality control on the supply side and quality assurance on the user side have been overlooked in many countries, strengthening healthcare professionals' distrust of laboratory test results [47, 48]. As more expensive tests are decentralized, the costs of poor test performance and healthcare professionals' ignoring a test result because of distrust is a much bigger waste of precious resources. This is an extremely complex process to address, given the breadth of end users in any national program for POC testing, making design of the program and distribution difficult. The training and use of dried blood spots for serology, HIV load, and enzyme-linked immunospot assays and dried culture spots for tuberculosis diagnosis has helped to establish a more uniform practice to some of these processes.

Resources must be dedicated to implementing sustainable quality control and external quality assessment systems. The development of setting-appropriate control panels (with long shelf lives and affordable prices, preferably without cold-chain distribution) that can inform these quality assurance systems has lagged significantly. The implementation and assurance for new POC platforms would definitely benefit from quality control and external quality assessment throughout the life of the system [49, 50].

OPPORTUNITIES TO REDUCE BARRIERS

Solutions to these barriers require different kinds of interventions.

1. Policy. Treatment guidelines that clearly define the role of diagnostics in informing patient management or programmatic decisions can play a big role in defining markets, by reducing a level of uncertainty on the supply side and thus incentivizing the development of innovative diagnostics. One example has been the level of effort put into developing more field-friendly CD4 cell count tests, leading to decentralization of testing for decision making about when to start and when to switch ART. In contrast, innovation for POC viral load testing has lagged behind, in part because of a lack of market incentive. From a market perspective, traditionally, the cost of and performance criteria for CD4 cell count testing have been lower and more clearly defined, respectively, than for viral load testing. Clear performance criteria for diagnostic tests that reflect appropriate and clinically relevant standards would accelerate both innovation and implementation.

2. System and Human Capacity Strengthening. Fundamentally, the ability of countries to assess new technologies and adopt and implement them effectively requires significant human capacity and health systems strengthening at multiple levels: regulatory, procurement, distribution, laboratory, quality, health, and information systems [26]. One approach to address this complex network of systems and leverage vertical funding opportunities is through the development of national laboratory strategic plans, which lay the groundwork for integrated national laboratory systems [51, 52]. Several countries are at different stages of establishment and implementation of these strategic plans. These efforts are not trivial and require the involvement and alignment of multiple stakeholders and partners [51]. Another approach could be regional regulatory bodies that help assess and recommend technologies and plans for multiple countries and settings within their region.

3. Laboratory Information-Management Systems (LIMS). The full potential impact of a diagnostic test is dependent on an effective LIMS. Implementation of such systems requires significant resource investment and maintenance. The emergence of more robust, portable, and cost-effective hardware, along with the expansion of Internet and mobile telephone coverage, have greatly expanded the opportunities to address some of the challenges of existing LIMS. In the first instance, integration of laboratory test results with electronic medical records may provide healthcare professionals with access to test results more promptly and efficiently [53, 54]. Integration of delivery of laboratory results with electronic medical records has had a positive effect on the impact of laboratory testing in informing patient management [55–57]. In the past, from a laboratory systems' perspective, any form of instrumentation was perceived as a negative attribute for a decentralized test in low-resource settings. Today, this need no longer be the case. Electronic hardware has evolved to allow for more efficient transmission of information/data at a very low cost. Instruments can extend connectivity to the LIMS by providing test results to end users, test and instrument performance data to manufacturers and laboratory system managers, establishment of protocol, a history of quality control, and an inventory of reagent consumption (Figure 2). Standards for POC connectivity need to be developed.

4. Technology. Beyond the development of novel diagnostic tests and platforms with improved attributes and features, technology gaps remain. Following the example of CD4 cell count testing above, innovation for POC viral load testing has lagged behind, in part because of specific technological constraints. From a technological perspective, NAT-based platforms, such as those based on polymerase chain reaction, for target amplification have been difficult to re-engineer as small battery-operated stand-alone systems and have proven to be prone to contamination outside of a pristine reference laboratory environment. However, new programs have been initiated to incentivize innovation for NAT that surmounts these technological barriers. Stable control reagents for external quality assessment and quality control programs remain a significant technological gap and must be addressed to support POC testing. The development of novel training tools that use the newly available information technologies to ensure appropriate training and proficiency may well be an opportunity to address major problems with implementation of POC diagnostic tests.

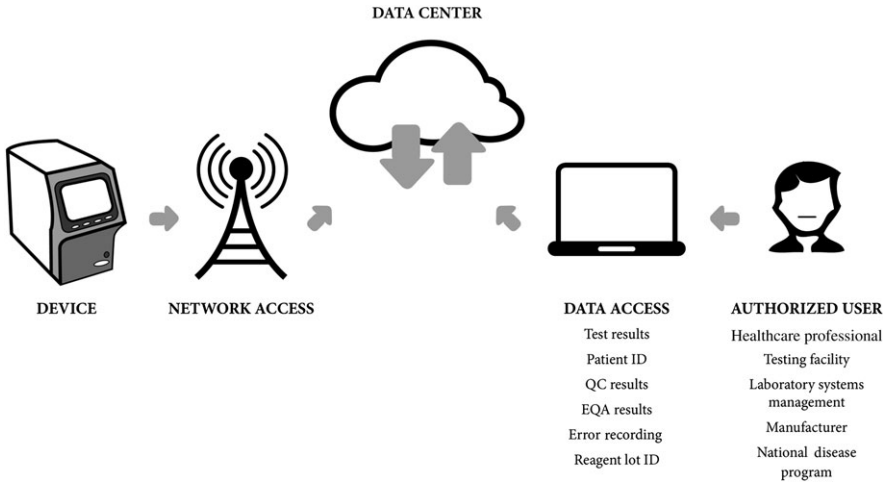

Figure 2. The opportunity for devices at the point-of-care to interface and extend the laboratory information management systems. Connectivity allows real-time and automated data and information exchange to different end users. Abbreviations: EQA, external quality assessment; ID, identification; QA, quality assurance.

CONCLUSIONS

The primary beneficiaries of POC diagnostics are the patients living in remote areas with limited access to the healthcare system. Interestingly, while patients do play a role in market research and user-needs studies, there are few mechanisms to involve patient advocacy groups in programmatic decisions regarding diagnostic testing. Biosafety, specimen processing, and stability constraints mean that patients with HIV infection and/or tuberculosis must often travel further to provide clinical specimens for testing than to receive treatment [58]. Distance from the patient's home to the specimen collection site is directly correlated to the direct and opportunity costs borne by the patient, particularly in rural and remote areas [59]. POC diagnostics will have the most impact in the areas that central laboratory testing systems cannot efficiently service. These are also the most challenging areas in which to introduce new technologies. Beyond these challenges, there are market uncertainties in many processes that are key to the introduction of new technologies, including regulatory approval, inconsistencies in purchasing practices, inconsistencies in performance specifications, mechanisms for nongovernmental organizations to approve and endorse the technologies, and the ability and willingness of the donor community and national programs to pay. From the supply perspective, these uncertainties result in untenable uncertainty in timelines for product introduction and scale-up, with unpredictable market return on investment. Critically, there is a need for clear policy relating performance criteria to clinical decision making, as well as for a more agile and responsive regulatory framework to serve countries that do not have these in place. From the demand perspective, the deciding factor for introducing a new test in the public sector should be its health systems impact, of which test performance is just one component within the context of broader program priorities [60].

A major challenge for global stakeholders remains: how to pave the road for timely introduction of innovative technologies on the basis of the appropriateness and impact of the technologies.

Notes

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